Attorney for Applicants
Sara D. Vinarov, Reg. No. 48,524
TEL 608-251-5000
FAX 608-251-9166

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Alan D. Attie
Jonathan P. Stoehr
Kathryn L. Schueler
Susanne Michelle Clee

Date: January 21, 2008

Serial No.: 10/655,915

Group Art Unit: 1634

Filed: 09/05/2003

Examiner: Jehanne Souaya Sitton

Title: TYPE 2 DIABETES SUSCEPTIBILITY GENES

File No.: 960296.99080

Confirmation No.: 8862

DECLARATION OF SUSANNE MICHELLE CLEE
Under 37 CFR 1.132

Commissioner for Patents
P O Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Susanne Michelle Clee, on oath declare and sayeth that:

1. I am the same Susanne Michelle Clee who is a named co-inventor on the above-identified patent application. I make this declaration in support of that patent application. I am currently employed by the University of British Columbia as an Assistant Professor in the Department of Cellular and Physiological Sciences. I have worked as a scientist for 12 years specializing in the genetics of complex diseases. I have published extensively in this area. A copy of my *Curriculum Vitae* is attached as Exhibit A.

2. I have reviewed the above-identified application and understand the nature and scope of the invention claimed therein. I have also reviewed the Office Action issued by the U.S. Patent and Trademark Office (USPTO) on July 31, 2007 for this application. I understand that currently Claims 1-3, and 12 stand rejected as failing to comply with the USPTO's enablement and written description requirements. I also understand that these rejections are largely due to the fact that Table 1, pg. 4, [00018] of the application contains an inadvertent

numbering error in the 1st row, 4th column ("position in protein"). An attempt was made to correct Table 1 in previous responses, however, the USPTO issued a "new matter" rejection asserting that the numbering correction was not supported by the original application as filed. I disagree with this rejection.

3. I believe that the numbering error, notably at amino acid position 52 in Table 1 does not constitute new matter. I also believe that not only would one of ordinary skill in this art recognize the existence of the error based on the specification as a whole, but one would also recognize the appropriate correction. Thus, correction of the amino acid position in the 1st row, 4th column of Table 1 from "50" to "52", which corresponds to nucleotide position 172 in the cDNA would have been immediately obvious to one of ordinary skill in the art at the time of filing.

4. As support for this belief, I submit that the following information was provided in the specification at the time of filing:

a) Mouse SorCS1 nucleotide (nt) sequence is disclosed as GenBank Accession No. AF195056 (see specification pg. 6, paragraph 25, last line). A copy of GenBank Accession No. AF195056 is provided herewith as Exhibit B. Mouse SorCS1 nucleotide sequence shows that the 1st initiation codon, ATG (Met) corresponds to nucleotides 18-20. The 5'untranslated region (UTR) is 17 nucleotides in length. From the 1st nucleotide in the 1st amino acid ATG (Met) to nucleotide 172 (location of the substitution, the 2nd nucleotide of the Thr at position 52), there are 155 nucleotides (172nt - 17nt in 5'UTR = 155nts).

b) Human SorCS1 nucleotide sequence is disclosed as GenBank Accession No. NM_052918 and amino acid sequence as GenBank Accession No. NP_443150 (see specification pg. 5, paragraph 19, and enclosed Exhibit C).

c) The Sequence Listing in the specification includes SEQ ID NOs. 3 and 4.

i) SEQ ID NO. 3 is the human SorSC1 nucleotide sequence, which discloses that the 5'UTR is 8 nucleotides in length. The 1st amino acid is a Met and it corresponds to nucleotides 9-11 (ATG). 155 nucleotides from the 1st

nucleotide in the 1st amino acid (Met) is the 2nd nucleotide in the Thr at position 52, which corresponds to position 163 in the human cDNA (155 nt + 8 nt in 5'UTR = 163 nts).

ii) SEQ ID NO. 4 is the human SorSC1 amino acid sequence, which discloses a Thr (ACC) at position 52, but not position 50 (Ala).

d) Figure 2A-H in specification provides an amino acid sequence alignment for mouse SorCS1a, b, c (SEQ ID NOs: 11-13) and human SorCS1 (SEQ ID NO: 14). For mouse and human SorSC1 amino acid sequences, there is a T (Thr) at position 52. As shown in SEQ ID NO. 4 and Figure 2, in human SorCS1 there is an Ala at amino acid 50, not a Thr.

5. Based on the above information provided in the specification, one of skill in the art would readily recognize that the published mouse 5'UTR is 17 nucleotides in length and the published human 5'UTR is 8 nucleotides in length. The difference in the untranslated regions of the two species is 9 nucleotides. The published mouse and human coding sequences show that the number of nucleotides from the first nucleotide (A, adenine) of the first amino acid (Met) to the substituted nucleotide in the amino acid in question must be 155 nucleotides. Due to the different lengths of the 5'UTR, in mouse, amino acid position 52 corresponds to nucleotides 171, 172 and 173 (ACC). In human, amino acid position 52 corresponds to nucleotides 162, 163 and 164 (ACC). (Underlining shows the corresponding change in the nucleotide).

6. Based on the published mouse SorSC1 sequence, the 5'UTR is 17 nucleotides in length, and the total length from the beginning of the 5'UTR to the substituted nucleotide in the amino acid in question is 172 nucleotides long. Therefore, the coding sequence from the 1st nucleotide of the first amino acid to the substituted nucleotide in the amino acid in question is 155 nucleotides (172nt – 17nt).

7. Since an amino acid is made up of 3 nucleotides, 155 nucleotides would equal 51amino acids (153 nt) plus 2 nucleotides. These 2 nucleotides are the first 2 nucleotides of the amino acid at position 52 of the published mouse SorSC1 sequence.

8. I submit that in the first row, first column of Table 1, the number 172 is the substituted nucleotide position in the mouse SorSC1 sequence. The C to T in the 2nd and 3rd column, first row of Table 1, denote the substitution in the 2nd nucleotide of the amino acid that is the subject matter of the pending claims. The number 50 in column 4, first row of Table 1 denotes the location of the amino acid that contains the above mentioned substitution in the 2nd nucleotide. The coding sequence from the 1st nucleotide of the 1st amino acid to the substituted nucleotide in the amino acid in question (number 50) is 149 nucleotides, not the 155 nucleotides dictated by a mutation at nucleotide 172.

9. One skilled in the art would immediately recognize that the number "50" as the position of the mutation in the mouse SorCS1 sequence is clearly wrong. This is because the published mouse SorSC1 sequence has a 5'UTR that is 17 nucleotide in length, and the total length from the beginning of the 5'UTR to the substituted nucleotide in the amino acid in question is 172 nucleotides long. In mouse, the number of SorSC1 nucleotides in the coding sequence from the 1st nucleotide of the 1st amino acid to the substituted nucleotide in the amino acid in question is 155 nucleotides. The difference between 149 and 155 is 6 nucleotides which would immediately alert one skilled in the art that the difference is 2 amino acids. Therefore, the amino acid in question should be 52 not 50.

10. Further, in the published human SorSC1 sequence, the 5'UTR is 8 nucleotides in length, and the total length from the beginning of the 5'UTR to the substituted nucleotide in the amino acid in question is 163 nucleotides long. The coding sequence from the 1st nucleotide of the 1st amino acid to the substituted nucleotide in the amino acid in question is still 155 nucleotides. This means that similar to the above analysis for the mouse SorSC1 sequence, the human SorCS1 sequence with 155 nucleotides in length equals 51amino acids plus 2 nucleotides. These 2 nucleotides are the first 2 nucleotides of the amino acid at position 52 of the published human SorSC1 sequence. Like, the mouse SorSC1 analysis, one skilled in the art would immediately realize that in the human sequence the amino acid in question is also "52" not "50."

11. For the sake of argument, even if one skilled in the art were to use the number 50 in the first row, column 4 of Table 1, as the amino acid that contains the substitution in the 2nd

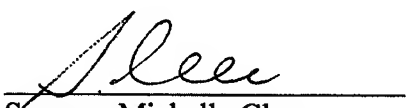
nucleotide, the coding sequence from the 1st nucleotide of the 1st amino acid to the substituted nucleotide in the amino acid in question would be 149 nucleotides. One skilled in the art would immediately recognize that the number "50" in Table 1 is a sequence error because 1) the published mouse SorSC1 sequence has a 5'UTR that is 17 nucleotides in length, and 2) the total length from the beginning of the 5'UTR to the substituted nucleotide in the amino acid in question is 172 nucleotides long. Therefore, the coding sequence from the 1st nucleotide of the 1st amino acid to the substituted nucleotide in the amino acid in question is 155 nucleotides.

12. The difference in the number of nucleotides between 149 and 155 is 6. One skilled in the art would immediately recognize this difference of 6 nucleotides translates into a difference of 2 amino acids. This would make the amino acid position in table 1, which is in question, "52" not "50." Therefore, I believe that correction of the amino acid position in the 1st row, 4th column of Table 1 from "50" to "52" corresponding to nucleotide position 172 in the mouse SorCS1 cDNA would have been immediately obvious to one of ordinary skill in the art at the time of filing.

13. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Further declarant sayeth not.

Dated: January 21, 2008



Susanne Michelle Clee

THE UNIVERSITY OF BRITISH COLUMBIA
Curriculum Vitae for Faculty Members

Date: **Initials:**

1. **SURNAME**: CLEE **FIRST NAME**: Susanne
MIDDLE NAME(S): Michelle

2. **DEPARTMENT/SCHOOL:** Department of Cellular and Physiological Sciences

3. **FACULTY**: Medicine

4. **PRESENT RANK**: Assistant Professor **SINCE**: August 2007

5. **POST-SECONDARY EDUCATION**

University or Institution	Degree	Subject Area	Dates
University of British Columbia, Canada	Ph.D.	Genetics	1995-2001
Simon Fraser University, Canada	B.Sc. (Hon)	Biochemistry	1990-1994

Title of Dissertation and Name of Supervisor

Lipoprotein lipase and the ATP binding cassette transporter ABCA1: Two genes regulating plasma high density lipoprotein cholesterol and triglyceride levels and risk of coronary artery disease.
Supervisor: Dr. Michael R. Hayden

Special Professional Qualifications

6. **EMPLOYMENT RECORD**

(a) Prior to coming to UBC

University, Company or Organization	Rank or Title	Dates
University of Wisconsin-Madison, Dept of Biochemistry	Assistant Scientist	7/2006-6/2007
University of Wisconsin-Madison, Dept of Biochemistry	Postdoctoral Fellow	9/2001-6/2006

(b) At UBC

Rank or Title	Dates
Assistant Professor	8/2007+

EXHIBIT
tabbies
A

(c) Date of granting of tenure at U.B.C.:

7. LEAVES OF ABSENCE

University, Company or Organization at which Leave was taken	Type of Leave	Dates

8. TEACHING

(a) Areas of special interest and accomplishments

(b) Courses Taught at UBC

Session	Course Number	Scheduled Hours	Class Size	Hours Taught			
				Lectures	Tutorials	Labs	Other

(c) Graduate Students Supervised and/or Co-Supervised

Student Name	Program Type	Year		Principal Supervisor	Co-Supervisor(s)
		Start	Finish		

(d) Continuing Education Activities

(e) Visiting Lecturer (indicate university/organization and dates)

(f) Other

9. SCHOLARLY AND PROFESSIONAL ACTIVITIES

(a) Areas of special interest and accomplishments
Genetics of metabolic diseases, in particular obesity and diabetes
Physiology of animal models of metabolic disease

(b) Research or equivalent grants (indicate under COMP whether grants were obtained competitively (C) or non-competitively (NC))

Granting Agency	Subject	COMP	$ Per Year	Year	Principal Investigator	Co-Investigator(s)
American Heart Association	Scientist Development Grant: *Identification of the Modifier of Obese 1 (Moo1) obesity gene*	C	65,000	7/06-6/10	Susanne M Clee	
American Heart Association	Postdoctoral Fellowship	C	35,000 (yr1) 40,000 (yr2)	7/05-6/06	Susanne M Clee	
American Heart Association	Postdoctoral Fellowship	C	51,048	7/03-6/05	Susanne M Clee	

(c) Research or equivalent contracts (indicate under COMP whether grants were obtained competitively (C) or non-competitively (NC).

Granting Agency	Subject	COMP	$ Per Year	Year	Principal Investigator	Co-Investigator(s)

(d) Invited Presentations

1. **Clee S.M.** Genotyping strategies for fine-mapping a diabetes QTL. Wisconsin Symposium III. Madison, WI May 20-23, 2003.
2. **Clee S.M.**, Attie A.D. The BTBR *ob/ob* model of type II diabetes. New Genetic and Metabolic Insights into Animal Models of Diabetes. Bar Harbor ME June 17-21, 2003.
3. **Clee S.M.**, Attie A.D. New genes for type II diabetes from genetic and genomic studies in mice. Washington University Lipid and Diabetes Symposium, St. Louis MO, Apr. 21, 2005.
4. **Clee S.M.** Positional cloning of a type 2 diabetes susceptibility gene: SorCS1, Marshfield Clinic, Marshfield WI, Sept. 2006.
5. **Clee S.M.** Genetics of obesity and type 2 diabetes, CIHR New Principal Investigator Meeting, Jackson's Pt. ON, Nov. 2007.

(e) Other Presentations (selected from abstracts, presenting author underlined)

1. Pimstone S. N., Gagne E., **Clee S. M.**, Stein E. A., and Hayden M. R. Post Prandial Retinyl Palmitate Response Supports Evidence for a Functional Effect of the Asn291Ser Mutation in the Lipoprotein Lipase Gene. *Oral presentation*, 68th Scientific Sessions of the American Heart Association, Anaheim CA Nov 13-16, 1995. *Circulation* 92 (8, Suppl.) I493. Oct. 15, 1995.
2. Pimstone S. N., Hayden M. R., **Clee S. M.**, Bakker H. D., Kastelein J. J. P. and Defesche J. C. Familial Defective Apolipoprotein B: Evidence For a Milder Phenotype in Children. *Poster*, 66th Congress of the European Atherosclerosis Society, Florence Italy July 13-17, 1996.
3. **Clee S. M.**, Zhang H., Benlian P., Miao L., Bissada N., Shen G. X., Angel A., LeBoeuf R. C., and Hayden M. R. Lipoprotein Lipase Increases HDL Cholesterol Levels in Mice Expressing Cholesterol Ester Transfer Protein. *Oral presentation*, Pacific Northwest Lipid Club, Seattle WA, Oct. 11-12, 1996.
4. **Clee S. M.**, Zhang H., Benlian P., Miao L., Bissada N., Shen G. X., Angel A., LeBoeuf R. C., and Hayden M. R. Lipoprotein Lipase Increases HDL Cholesterol Levels in Mice Expressing Cholesterol Ester Transfer Protein. *Oral presentation*, 69th Scientific Sessions of the American Heart Association, New Orleans LA Nov 10-13, 1996. *Circulation* 1996 **94** (8, Suppl.): I399.
5. **Clee S. M.**, Ginzinger, D. G., Excoffon, K. J. D. A., Backus, R. C., Lewis, M. E. S., Jones, B., Rogers, Q. R., and Hayden M. R. Decreased Adipose Tissue and Tolerance of High Fat/High Cholesterol Feeding Despite Massive Hypertriglyceridemia in Cats Homozygous for LPL Deficiency. *Poster*, Enzymes, Receptors, and Drugs in Obesity and Atherosclerosis, Toronto, ON May 7-9, 1998. *Clinical Biochemistry* 1998 **31**:601.
6. **Clee, S. M.**, Bissada N., Miao F., Miao L., Steures P., Marais A. D., McManus J., McManus B., Henderson H. E., and Hayden M. R. Atherogenicity of Lipoprotein Lipase is Related to Its Site of Expression: *In Vivo* Evidence of Vessel Wall versus Plasma Effects. *Oral presentation,* Canadian Lipoprotein Conference, Muskoka ON. Oct. 16-19, 1998.
7. **Clee S. M.**, Wittekoek M. E., Loubser O., Collins J., Moll E., Pimstone S. N., Kastelein J. J. P. and Hayden M. R. Common Variants of Lipoprotein Lipase (LPL) Strongly Influence Levels of Lipids and Lipoproteins and Coronary Artery Disease (CAD) in Patients with Familial Hypercholesterolemia (FH). *Poster presentation,* Canadian Lipoprotein Conference, Muskoka ON. Oct. 16-19, 1998.
8. **Clee, S. M.**, Bissada N., Miao F., Miao L., Steures P., Marais A. D., McManus J., McManus B., Henderson H. E., and Hayden M. R. Atherogenicity of Lipoprotein Lipase is Related to Its Site of Expression: *In Vivo* Evidence of Vessel Wall versus Plasma Effects. *Poster presentation*, 71st Scientific Sessions of the American Heart Association, Dallas TX Nov. 8-11, 1998. *Circulation* 1998 98(17):I-531
9. Kastelein J. J. P., Wittekoek M. E., Loubser O., **Clee S. M.**, Collins J., Moll E., Pimstone S. N., and Hayden M. R. Common Variants of Lipoprotein Lipase (LPL) Strongly Influence Levels of Lipids and Lipoproteins and Coronary Artery Disease (CAD) in Patients with Familial Hypercholesterolemia (FH). *Oral presentation*, 71st Scientific Sessions of the American Heart Association, Dallas TX Nov. 8-11, 1998. *Circulation* 1998 98(17):I-739.
10. **Clee, S. M.**, Loubser O., Wittekoek M. E., Collins J., Pimstone S. N., Moll E., Kastelein J. J. P. and Hayden M. R. Common Variants of Lipoprotein Lipase (LPL) Strongly Influence Lipid Levels, Blood Pressure and

Coronary Artery Disease in Patients with Familial Hypercholesterolemia. *Poster presentation*, Canadian Genetic Diseases Network Annual Scientific Meeting, Collingwood ON April 20-23, 1999.

11. **Clee, S. M.**, Marcil M., Brooks-Wilson A., Roomp K., Zhang L., Yu L., Collins J.A., van Dam M., Loubser O., Ouellette B.F.F., Sensen C. W., Fichter K., Mott S., Denis M., Pimstone S., Kastelein J.J.P., Genest J. Jr., Hayden M.R. Familial HDL deficiency with defective cholesterol efflux is caused by mutations in CERP (ABC1). *Oral presentation*, Canadian Lipoprotein Conference, Mont-Tremblant PQ Oct. 15-18, 1999
12. Brooks-Wilson A., Marcil M., **Clee S. M.**, Zhang L.-H., Roomp K., van Dam M.J., Yu L., Brewer C., Collins J.A., Molhuizen H.O.F., Ouellette B.F.F., Sensen C.W., Martindale D., Frohlich J., Morgan K., Koop B., Pimstone S., Kastelein J.J.P., Genest J. Jr., Hayden M.R. Mutations in transportin (ABC1) in Tangier disease and familial HDL deficiency. *Oral presentation*, American Society of Human Genetics, San Francisco CA, Oct. 19-23, 1999. *American Journal of Human Genetics* 1999 65(4 suppl):A34.
13. **Clee S. M.**, Loubser O., Collins J., Kastelein J. J. P, and Hayden M. R. The lipoprotein lipase S447X variant is associated with decreased systolic and diastolic blood pressure. *Poster presentation*, 72nd Scientific Sessions of the American Heart Association, Atlanta GA Nov. 7-10, 1999. *Circulation* 1999 100(18):I822.
14. **Clee S.M.**, Zwarts K.Y., Roomp K., Collins J.A., Marcil M., van Dam M., Brooks-Wilson A., Genest J. Jr., Kastelein J.J.P., and Hayden M.R. HDL levels in ABCA1 heterozygotes are predicted by cholesterol efflux levels and are influenced by age. *Poster presentation*, American Society of Human Genetics 50th annual meeting, Philadelphia PA Oct 3-7, 2000. *American Journal of Human Genetics* 2000 67(4 Suppl 2):350.
15. Molhuizen H.O.F., **Clee S.M.**, Zwinderman A.H., Engert J., Zwarts K.Y., Brooks-Wilson A., Hudson T., Jukema J.W., Kastelein J.J.P., and Hayden M.R. cSNP analysis of the ABCA1 gene: the R219K variant is associated with a blunted age-modulated increase in HDL cholesterol and decreased coronary artery disease (CAD). *Poster presentation*, American Society of Human Genetics 50th annual meeting, Philadelphia PA Oct 3-7, 2000. *American Journal of Human Genetics* 2000 67(4 Suppl 2):233.
16. **Clee S.M.**, Molhuizen H.O.F., Zwinderman A.H., Engert J., Roomp K., Jukema J.W., Zwarts K.Y., Rieder M.J., Nickerson D.A., Hudson T., Kruglyak L., Brooks-Wilson A., Genest J. Jr., Kastelein J.J.P., and Hayden M.R. Complete cSNP analysis of the ABC1 gene and association of the R219K variant with altered lipoproteins and risk of CAD. *Oral presentation*, Canadian Lipoprotein Conference, White Rock BC Oct 22-29, 2000.
17. Wellington C.L., **Clee S.M.**, Kwok A., Marcil M., Singaraja R., Kastelein J.J.P., Genest J. Jr., and Hayden M.R. Upregulation of ABC1 protein by 9-cis-retinoic acid, 22-R-OH-cholesterol is inhibited by truncation mutations. *Poster presentation*, 25th Annual Canadian Lipoprotein Conference, White Rock BC Oct 22-29, 2000.
18. **Clee S.M.**, Zwarts K.Y., Roomp K., Collins J.A., van Dam M., Marcil M., Brooks-Wilson A., Genest J. Jr., Kastelein J.J.P., and Hayden M.R. The age modulated phenotype in heterozygotes for mutations in ABC1 includes significantly decreased HDL, increased triglycerides and an increased frequency of coronary artery disease (CAD). *Oral presentation*, 73rd Scientific Sessions of the American Heart Association, New Orleans LA Nov. 12-15, 2000. *Circulation* 2000 102 (18):II-31.
19. **Clee S.M.**, Molhuizen H.O.F., Zwinderman A.H., Engert J.C., Roomp K., Zwarts K.Y., Jukema J.W., Hudson T.J., Brooks-Wilson A., Kastelein J.J.P., and Hayden M.R. cSNPs within the ABC1 gene influence HDL cholesterol levels and risk of coronary artery disease (CAD). *Poster presentation*, 73rd Scientific Sessions of the American Heart Association, New Orleans LA Nov. 12-15, 2000. *Circulation* 2000 102 (18):II-278.
20. **Clee S.M.**, Zwarts K.Y., Zwinderman A.H., Engert J.C., Roomp K., Jukema J.W., Hudson T.J., Brooks-Wilson A., Kastelein J.J.P., and Hayden M.R. *ABCA1* regulatory variants influence CAD independent of effects on plasma lipid levels. *Oral presentation*, 74th Scientific Sessions of the American Heart Association, Anaheim CA Nov. 11-14, 2001. *Circulation* 2001 104 (17):2131. (unable to present due to illness)
21. Wellington C.L., Yang Y.Z., Kwok A., **Clee S.M.**, Zwarts K., Marcel M., Newman S., Roomp K., Singaraja R., Zhang L.H., Kastelein J.J.P., Genest J., and Hayden M.R. Truncation mutations in human ABCA1 suppress normal upregulation of wild-type ABCA1 by 9-cis-retinoic acid and 22-R-hydroxycholesterol. *Oral presentation*, 74th Scientific Sessions of the American Heart Association, Anaheim CA Nov. 11-14, 2001. *Circulation* 2001 104 (17):1397.
22. Singaraja R.S., Fievet C., Castro G., James E., **Clee S.**, Hennuyer N., Choy J., Bissada N., McManus B., Staels B., and Hayden M.R. Increased HDL and changes in lipoprotein composition are associated with increased efflux and atheroprotection in an *ABCA1* BAC transgenic mouse model. *Oral presentation*, 75th Scientific Sessions of the American Heart Association, Chicago IL Nov. 17-20, 2002. *Circulation* 2002 106 (19):219.
23. **Clee S.M.**, Stoehr J.P., Rabaglia M.E., Schueler K. L., and Attie A.D. Fine-Mapping of a type-II diabetes gene. *Oral presentation*, Keystone Symposium Toward Understanding Islet Biology, Keystone CO, Jan. 21-26, 2003.

24. **Clee S.M.**, Stoehr J.P., Rabaglia M.E., Schueler K. L., and Attie A.D. Fine-mapping and characterization of a type-II diabetes gene. *Oral presentation*, Wisconsin Symposium III, Madison WI, May 20-23, 2003.
25. **Clee S.M.**, Gray-Keller M., Rabaglia M.E., Stapleton D., Raess P.W., and Attie A.D. The BTBR-*ob/ob* model of type II diabetes is characterized by ultrastructural abnormalities consistent with impaired mitochondrial function. *Poster presentation*, Keystone Symposium Diabetes Mellitus: Molecular Mechanisms, Genetics and New Therapies, Keystone CO, Jan. 27-Feb. 2, 2005.
26. **Clee S.M.**, Yandell B., Schueler K.M., Taylor K.D., Goodarzi M.O., Rabaglia M.E., Kabara E.A., Klass D.M., Stapleton D.S., Guo X., Cui J., Stoehr J.P., Lan H., Quinones M.J., Hsueh W.A., Gray-Keller M.P., Boronenkov I., Raines S.M., Young M.B., Raess P.W., Flowers M.T., Rotter J.I., and Attie A.D. Positional cloning of a type II diabetes susceptibility gene: *SorCS1*. *Poster presentation*, Keystone Symposium Diabetes Mellitus and the Control of Cellular Energy Metabolism, Vancouver BC, Jan. 21-26, 2006.
27. **Clee S.M.**, Yandell B., Schueler K.M., Taylor K.D., Goodarzi M.O., Rabaglia M.E., Kabara E.A., Klass D.M., Stapleton D.S., Guo X., Cui J., Stoehr J.P., Lan H., Quinones M.J., Hsueh W.A., Gray-Keller M.P., Boronenkov I., Raines S.M., Young M.B., Raess P.W., Flowers M.T., Rotter J.I., and Attie A.D. Positional cloning of a type II diabetes susceptibility gene: *SorCS1*. *Poster presentation*, Wisconsin Symposium on Human Biology, Madison WI, May 22-25, 2006.
28. **Clee S.M.**, Yandell B., Schueler K.M., Taylor K.D., Goodarzi M.O., Rabaglia M.E., Kabara E.A., Klass D.M., Stapleton D.S., Guo X., Cui J., Stoehr J.P., Lan H., Quinones M.J., Hsueh W.A., Gray-Keller M.P., Boronenkov I., Raines S.M., Young M.B., Raess P.W., Flowers M.T., Rotter J.I., and Attie A.D. Positional cloning of a type II diabetes susceptibility gene: *SorCS1*. *Poster presentation (late breaking)*, American Diabetes Association 66th Scientific Sessions, Washington DC, June 9-13, 2006. *Diabetes* 2006.

(f) Other

(g) Conference Participation (Organizer, Keynote Speaker, etc.)

10. SERVICE TO THE UNIVERSITY

(a) Memberships on committees, including offices held and dates

(b) Other service, including dates

11. SERVICE TO THE COMMUNITY

(a) Memberships on scholarly societies, including offices held and dates

- Member, Canadian Obesity Network (2006+)
- Member, Canadian Diabetes Association (2007+)

(b) Memberships on other societies, including offices held and dates

(c) Memberships on scholarly committees, including offices held and dates

(d) Memberships on other committees, including offices held and dates

(e) Editorships (list journal and dates)

(f) Reviewer (journal, agency, etc. including dates)

- *Clinical Genetics* (2001+)
- *Physiological Genomics* (2007+)
- *Genome Biology* (2007+)

(g) External examiner (indicate universities and dates)

(h) Consultant (indicate organization and dates)

- Xenon Genetics Inc. (Now Xenon Pharmaceuticals, Inc.) 2000-2002

(i) Other service to the community

12. AWARDS AND DISTINCTIONS

(a) Awards for Teaching (indicate name of award, awarding organizations, date)

(b) Awards for Scholarship (indicate name of award, awarding organizations, date)

- American Heart Association Postdoctoral Fellowship 2005-2006
- Keystone Symposia Scholarship, 2005
- American Heart Association Postdoctoral Fellowship 2003-2005
- Keystone NIH Scholarship, 2003

(c) Awards for Service (indicate name of award, awarding organizations, date)

(d) Other Awards

13. OTHER RELEVANT INFORMATION (Maximum One Page)

THE UNIVERSITY OF BRITISH COLUMBIA
Publications Record

SURNAME: CLEE **FIRST NAME**: Susanne **Initials**:
MIDDLE NAME(S): M **Date**:

1. REFEREED PUBLICATIONS

(a) Journals

1. Kelly N., **Clee S.**, and Nakielna, B. Bioactive Tumor Necrosis Factor in the Sputum of Cystic Fibrosis Patients. *Clinical and Diagnostic Lab. Immunol.* 1995 **2**:499-502.
2. Zhang H., Henderson H., Gagne S. E., **Clee S. M.**, Miao L., Liu G., and Hayden M. R. Common Sequence Variants of Lipoprotein Lipase: Standardized Studies of In Vitro Expression and Catalytic Function. *Bioch. Biophys. Acta* 1996 **1302**:159-166.
3. Pimstone S. N., **Clee S. M.**, Gagne S. E., Miao L., Zhang H., Stein E. A., and Hayden M. R. A Frequently Occurring Mutation in the Lipoprotein Lipase Gene (Asn291Ser) Results in Altered Postprandial Chylomicron Triglyceride and Retinyl Palmitate Response in Normolipidemic Carriers. *J. Lipid Res.* 1996 **37**:1675-1684.
4. Pimstone S. N., Defesche J. C., **Clee S. M.**, Bakker H. D., Hayden M. R., and Kastelein J. J. P. Differences in the Phenotype Between Children With Familial Defective Apolipoprotein B-100 and Familial Hypercholesterolemia. *Arterioscler. Thromb. Vasc. Biol.*1997 **17**:826-833.
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(b) Conference Proceedings

(c) Abstracts

1. Pimstone S. N., Gagne E., **Clee S. M.**, Stein E. A., and Hayden M. R. Post Prandial Retinyl Palmitate Response Supports Evidence for a Functional Effect of the Asn291Ser Mutation in the Lipoprotein Lipase Gene. 68th Scientific Sessions of the American Heart Association. *Circulation* 1995 92 (8, Suppl.):I493.
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(d) Other

2. NON-REFEREED PUBLICATIONS

(a) Journals

Editorial Review only

1. Hayden M. R., **Clee S. M.**, Brooks-Wilson A., Genest Jr. J., Attie A. and Kastelein J.J.P. Cholesterol Efflux Regulatory Protein (CERP), Tangier Disease and Familial HDL Deficiency. *Curr. Opin. Lipidol.* 2000 **11**:117-122.
2. **Clee S.M.** Getting at the heart of coronary disease. *Clin. Genet.* 2004 **65**:347-9.
3. **Clee S.M.** Genomics goes to the dogs. *Clin. Genet.* 2004 **65**:349-351.
4. **Clee S.M.** Expressing the nature of quantitative traits. *Clin. Genet.* 2005 **68**:1-5.
5. **Clee S.M.** Sweet successes in diabetes genetics. *Clin. Genet.* 2007 **72**:83-86.

(b) Conference Proceedings

1. **Clee S.M.**, Nadler S.N., and Attie A.D. Genetic and genomic studies of the BTBR *ob/ob* mouse model of type 2 diabetes. *Am. J. Ther.* 2005 **12**:491-8.

(c) Other

3. BOOKS

(a) Authored

(b) Edited

(c) Chapters

4. PATENTS

1. **Clee S.M.**, Brooks-Wilson A.R., Hayden M.R., and Pimstone S.N. Compositions and methods for modulating HDL cholesterol and triglyceride levels. Published Mar. 8, 2001. Publication # WO 01/15676 A2.
2. Hayden M.R., Zwarts K.Y., and **Clee S.M.** Diagnostic methods for cardiovascular disease, low HDL-cholesterol levels and high triglyceride levels. Published Dec. 5, 2002. Publication # WO 02/097123 A2.

5. SPECIAL COPYRIGHTS

6. ARTISTIC WORKS, PERFORMANCES, DESIGNS

7. OTHER WORKS

8. WORK SUBMITTED (including publisher and date of submission)

9. WORK IN PROGRESS (including degree of completion)

1. **Clee S.M.**, Rabaglia M.E., Schueler K.M., Stapleton D.S., Yandell B.S., Ranheim T., Gray-Keller M.P., Raess P.W., and Attie A.D. *Obese* BTBR mice are a model of altered β-cell dynamics leading to severe type 2 diabetes. (formatting for resubmission, expected submission Jan 08)

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Entry View

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Go To: General Description References Features Sequence

General Information About The Entry

Entry Name	**GENBANK:AF195056**
Identifier	**AF195056**
Accession #	AF195056
Molecule Type	mRNA
Sequence Length	3780
Entry Division	ROD (Rodent)
Sequence Version	AF195056.1
GI	7715915
Creation Date	08-MAY-2000

⊟ Description

Description	Mus musculus SorCSb splice variant of the VPS10 domain receptor SorCS (SorCS1a) mRI
Organism	Mus musculus
Organism Classification	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus.

⊟ References

1. Hermey,G. Schaller,H.C.; **Alternative splicing of murine SorCS leads to two forms c completely in their cytoplasmic tails** Biochim. Biophys. Acta 1491:350-354 (2000)
   PubMed 10760602
   Position 1-3780

2. Hermey,G.; **Direct Submission** Submitted (14-OCT-1999) Zentrum f. Molekulare Neuro Entwicklungsneurobiologie, Martinistr. 52, Hamburg 20246, Germany
   Position 1-3780

⊟ Features

Key	Location	Qualifier	Value
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EXHIBIT tabbies B

Tools

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translation MGKVGAGDGSSAGLSALLAGAGLLMLLAPGVCSSLSCCP PQHPS

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Characteristics Length:3780

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Comment Features Sequence

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ACCESSION   NM_052918
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KEYWORDS    .
SOURCE      Homo sapiens (human)
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  TITLE     The DNA sequence and comparative analysis of human chromosome 10
  JOURNAL   Nature 429 (6990), 375-381 (2004)
   PUBMED   15164054
REFERENCE   2  (bases 1 to 7272)
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EXHIBIT tabbies C

AUTHORS Hermey,G., Keat,S.J., Madsen,P., Jacobsen,C., Petersen,C.M. and Gliemann,J.
TITLE Characterization of sorCS1, an alternatively spliced receptor with completely different cytoplasmic domains that mediate different trafficking in cells
JOURNAL J. Biol. Chem. 278 (9), 7390-7396 (2003)
PUBMED 12482870
REMARK GeneRIF: human sorCS1 has three isoforms, sorCS1a-c, with completely different cytoplasmic tails and differential expression in tissues
REFERENCE 3 (bases 1 to 7272)
AUTHORS Hampe,W., Rezgaoui,M., Hermans-Borgmeyer,I. and Schaller,H.C.
TITLE The genes for the human VPS10 domain-containing receptors are large and contain many small exons
JOURNAL Hum. Genet. 108 (6), 529-536 (2001)
PUBMED 11499680
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from AF284756.1, BE019093.1, AY099452.1, AK125464.1 and AL133395.21.
On Mar 24, 2005 this sequence version replaced gi:18379341.

Summary: This gene encodes one family member of vacuolar protein sorting 10 (VPS10) domain-containing receptor proteins. The VPS10 domain name comes from the yeast carboxypeptidase Y sorting receptor Vps10 protein. Members of this gene family are large with many exons but the CDS lengths are usually less than 3700 nt. Very large introns typically separate the exons encoding the VPS10 domain; the remaining exons are separated by much smaller-sized introns. These genes are strongly expressed in the central nervous system. Two of the five family members (sortilin and sortilin-related receptor) are synthesized as preproproteins; it is not yet known if this encoded protein is also a preproprotein. Alternatively spliced transcript variants encoding different isoforms have been identified.

Transcript Variant: This variant (1) represents the longer transcript, but encodes the shorter isoform (a).
COMPLETENESS: complete on the 3' end.

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